UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,816	10/02/2003	Gordon Parry	53038AUSM1	3268

7590 07/10/2006

Wendy Washtien,
Berlex Biosciences, Patent Department
2600 Hilltop Drive Avenue
P.O. Box 4099
Richmond, CA 94804-0099

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 07/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,816	PARRY ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *1-47,57,66 and 70-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-56, 58-65 and 67-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/23/04; 2/14/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-85 are all the pending claims for this application.

Election/Restrictions

2. Applicant's election of Group 23 ("claims 48-65, 67-69 drawn to antibody and kits") in the reply filed on May 23, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Also, it is noted that none of the claims in Group 23 are drawn to kit(s) comprising an antibody- the only kit claim in the entire claim set is drawn to a nucleotide (Claim 85). The Examiner respectfully regrets that this appears to have been a typographical error in the description for Group 23 of the Restriction/Election of March 27, 2006.

In view of the Applicant's election of claims drawn to an antibody, the newly assigned Examiner reconsidered the elected claims and proposed re-restriction of claim 57 (drawn to an idiotypic antibody, Class 424, subclass 131.1) as new Group 37 of the Restriction/Election of March 27, 2006, as discussed in a telephonic interview with Applicants' representative, Ms. Wendy Washtein, on June 22, 2006. An interview summary is attached hereto.

The Examiner's grounds for re-restriction are based on the antibody of elected Group 23 and the idiotypic antibody of Group 37 being separate and distinct products having a materially different design, mode of operation, function or effect (MPEP §806.05(j)). The antibody of Group 23 binds to a modified hepsin molecule and the idiotypic antibody of new Group 37 binds to an anti-modified hepsin antibody. The

antibodies would have different amino acid sequences. Additionally, the antibodies are not obvious variants of each other based on the distinct structures and functions of each as noted above. To search Groups 23 and 37 together would present a search burden on the Examiner due to the extensive databases of patent and non-patent literature references. Thus, Groups 23 and 37 have been appropriately restricted on the basis of being both independent and presenting a search burden on the Examiner if they were to be searched together.

The Examiner gratefully acknowledges Applicants' telephone reply of June 26, 2006, consenting to the withdrawl (without traverse) of Claim 57 from the elected Group 23. Accordingly, Claims 48-56, 58-65 and 67-69 are all the claims under examination with claims 1-47, 57, 66 and 70-85 withdrawn for being non-elected subject matter.

Information Disclosure Statement

3. The U.S. and foreign patent literature references and the non-patent literature references cited in the IDSs of February 23, 2004 and February 14, 2005 have been considered and made of record.

It is noted that the IDS of February 14, 2005 lists an incorrect filing date for this application (i.e., October 3, 2003 instead of October 2, 2003), but otherwise appears to correspond to this application.

Specification

4. The specification is objected for the following:

a) Pursuant to 37 CFR 1.821, Applicants are required to provide sequence identifiers for any sequence ≥4 amino acids or ≥10 nucleic acids, and the following sequences are not properly identified:

p. 13, line 11, DDDDK-IVGG (SEQ ID NO: 3)

p. 13, lines 7 and 12, p. 16, line 27, p. 23, lines 8-9, RIVGG (SEQ ID NO: 32)

p. 70, lines 24-25, AGAGGCAGTGACATGGCGCAGAAGGAGGGT (SEQ ID NO: 10) and TGG AGG CTG CGC AGC GAG AAG (SEQ ID NO: 11)

p. 72, lines 12-14, TCGAGTCCCCATAATCAGCAA (SEQ ID NO: 12), CATCTTGGGCTTGATCTGGTTT (SEQ ID NO: 13), and ATGTCTGCAATGGCGCTGACTTCTATGG (SEQ ID NO: 14)

p. 72, lines 16-18, AGGTCATCTCCGTGTGTGATTG (SEQ ID NO: 15), CCCACGATGCGGTCCA (SEQ ID NO:16), CAGAGGCCGTTTCTTGGCCGC (SEQ ID NO: 17)

p. 77, lines 3-4, AGAGGCAGTGACATGGCGCAGAAGGAGGGT (SEQ ID NO: 18) and TGGAGGCTGCGCAGCGAGAAG (SEQ ID NO: 19)

p. 77, lines 22-23, CAGCTCGAATTCGGTAAGCCTATCCCT (SEQ ID NO: 20) and GATGCGGCCGCTTTAAACTCAATGGTG (SEQ ID NO: 21)

p. 77, lines 26-27, CATATGCCCGGGAGGAGTGACCAGGAG (SEQ ID NO: 22) and CTTACCGAATTCGAGCTGGGTCACCAT (SEQ ID NO: 23)

p. 78, lines 32-33, CTGATCCGGACAGGAGTGACCAGGAGCCGC (SEQ ID NO: 24) and GCCGGGTC CCAGGAAAGGA (SEQ ID NO: 25)

p. 79, lines 6-9, gatcgatatcgccaccatggagacagacacactcctgctat gggtactgctgctctgggttccagg (SEQ ID NO: 26) and atCgTCCGGAGCGTCACCAGTGGAACCT GGAACCCAGAGCAGCAGt (SEQ ID NO: 27)

p. 79, lines 32-33, GAGATCCGGACCAAG ACTGTGGCCGTAGGAAGCTG (SEQ ID NO: 28) and GCCGGGTCCCAGGAAAGGA (SEQ ID NO: 29)

p. 80, lines 10-11, TGCAGGTACCTAGGAGTGACCAGGAGCCGCTG (SEQ ID NO: 30) and CCGGGGTACCAGCTGGGTCACCATGCCGCTGGC (SEQ ID NO: 31)

b) The specification contains an omission for an ATCC deposit no. on p. 46, line 17.

c) The use of trademarks (e.g., BLUESCRIPT [BLUESCRIPT®]) has been noted in this application. A trademark should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

5. Claims 63 and 67-69 are objected to because of the following informalities:

a) Claim 63 is drawn to a hybridoma deposit but the ATCC deposit number has been omitted from the claim. This appears to be a typographical error. The specification teaches a second hybridoma cell line which is designated 94A7 (p. 46, line 16). If Applicants do not intend to claim the 94A7 hybridoma, then cancellation of the claim would overcome this objection. Appropriate correction is required.

b) Claims 67-69 are objected to for depending from non-elected claim 66.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 61 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 63 is indefinite for omitting to include the ATCC No. for the intended hybridoma. The specification teaches a second hybridoma cell line which is designated 94A7 (p. 46, line 16). See the Examiner's further comments under section 4, supra, and section 7, infra.

b) Claim 67 recites improper Markush group language and "a group" in line 2 should be amended to -- the group --.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 62 and 63 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (a) known and readily available to the public; (b) reproducible from the written description.

a. It is unclear if a hybridoma cell line which produces an antibody having the exact chemical identity of 14C7 (or 94A7) is known and publicly available, or can be reproducibly isolated without undue experimentation. The Examiner's search of the ATCC website did not reveal a deposit designated as PTA-4561 or under the name of the hybridoma, 14C7 (see copies of the search output). Additionally, a deposit for the hybridoma designated 94A7 does appear to have been made (see copy of search output). Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line(s), one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line(s); (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

b. For example, very different V_H chains (about 50% homologous) can combine

with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species without a hybridoma deposit. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809

regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same

as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 48-56, 58-61, 63-65 and 67-69 are rejected under 35 U.S.C. 102(e) as being anticipated by Mu et al. (US20030049645; published March 13, 2003; filed February 12, 2002; hereinafter referred to as "Mu").

Claims 48-56, 58-61, 63-65 and 67-69 are drawn to antibodies, fragments or derivatives with binding ability for a modified hepsin molecule, Fab, F(ab')2 or Fv fragment, polyclonal antibody or monoclonal antibody, recombinant protein comprising the antigen-binding region of the antibody, competes for binding to the same epitope,

chimeric antibody comprising a human and murine region, humanized, neutralizing, immunoconjugate comprising a therapeutic agent comprising cytotoxic agents such as ricin, diphteria toxin, Pseudomonas exotoxin (PE) A, PE40, and radioisotopes, hybridomas producing monoclonals, pharmaceutical compositions comprising the antibody and a carrier including water, emulsions, oil/water emulsion, wetting agents, sterile solutions, excipients, starch, sugar, gelatin, magnesium stearate, talc, vegetable fats or oils, and glycols, pharmaceutical compositions formulated as a liposome, polymeric composition, or polymer microsphere or a tablet, coated tablet, or capsule.

Mu discloses an antibody to hepsin protein or polypeptide portions thereof [0029]; monoclonal, polyclonal, single-chain and engineered antibodies (including humanized antibodies) and fragments, which specifically bind hepsin proteins and polypeptides; antibody fragments and single chain antibodies, that bind and "neutralize" hepsin proteins [0021]; antibodies generated against either the entire polypeptide or an antigenic fragment thereof [0058]; antibody fragments produced by the modification of whole antibodies, those synthesized de novo using recombinant DNA methodologies (for example, single chain Fv), humanized antibodies [0121]; polyclonal antibodies, monoclonal antibodies (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, $F(ab')_2$ fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments [0169]; monoclonals produced by hyrbidomas [0172]; chimeric antibodies comprising a mouse antibody molecule of appropriate antigen specificity and a human antibody molecule of appropriate biological activity [0173]; lipofectin or liposomes comprising the antibody, or

a fragment of the Fab region [0213]; pharmaceutical compositions comprising acceptable carriers or excipients [0218], and tablets or capsules or coated tablets [0219]; pregelatinised maize starch, polyvinylpyrrolidone, or hydroxypropyl methylcellulose [0219]; magnesium stearate, talc, or silica; disintegrants, for example, potato starch or sodium starch glycolate; wetting agents, for example, sodium lauryl sulphate [0219]; water; hydrogenated edible fats; emulsifying agents, for example, lecithin or acacia; non-aqueous vehicles, for example, almond oil, oily esters, ethyl alcohol, or fractionated vegetable oils [0219]; and preservatives, for example, methyl or propyl-p-hydroxybenzoate or sorbic acid; buffer salts and/or sweetening agents [0219]; gelatin and starch [0220]; emulsions in oily or aqueous vehicles, sterile pyrogen-free water [0221]; and polymeric or hydrophobic materials or ion exchange resins [0222].

Applicant is reminded that because the claims recite "comprising" language, any modified hepsin molecule is encompassed within the claim scope, and therefore anticipated by Mu. Also, because the hybridoma of Claim 63 has not been identified by an ATCC No. as discussed supra, any hybridoma producing an antibody against a modified hepsin molecule is encompassed by the claim scope, and therefore anticipated by Mu.

9. Claims 48-51, 53-55, 58-61, 63 and 64 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Brien et al. (US20040166117; published August 26, 2004; priority filing date of February 22, 2000; hereinafter referred to as "O'Brien").

The interpretation of Claims 48-51, 53-55, 58-61, 63 and 64 is discussed supra.

O'Brien discloses antibodies binding to hepsin peptide fragments [0050]; antibody specific for a hepsin fragment and binding [0056]; compounds having a targeting moiety and a therapeutic moiety, and wherein the targeting moiety is an antibody specific for hepsin and the therapeutic moiety is preferably a radioisotope, a toxin, a chemotherapeutic agent, an immune stimulant or cytotoxic agent [0057]; polyclonal antisera generated by using a fragment of hepsin as the immunogen in, e.g., rabbits. Standard protocols for monoclonal and polyclonal antibody production known to those skilled in this art are employed [0073]; intact anti-hepsin monoclonal antibody, but also an immunologically-active antibody fragment, e.g., a Fab or $(Fab)_2$ fragment; an engineered single chain Fv molecule; or a chimeric molecule, e.g., an antibody which contains the binding specificity of one antibody, e.g., of murine origin, and the remaining portions of another antibody, e.g., of human origin [0074]; the antibody, or a fragment thereof, may be linked to a toxin or to a detectable label, e.g., a radioactive label, non-radioactive isotopic label, fluorescent label, chemiluminescent label, paramagnetic label, enzyme label, or calorimetric label well-known in the art. Examples of suitable toxins include diphtheria toxin, Pseudomonas exotoxin A, ricin, and cholera toxin. Examples of suitable enzyme labels include alkaline phosphatase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, etc. Examples of suitable radioisotopic labels include ^{3}H, ^{125}I, ^{131}I, ^{32}P, ^{35}S, ^{14}C, etc. [0075].

Applicant is reminded that because the claims recite "comprising" language, any modified hepsin molecule is encompassed within the claim scope, and therefore anticipated by O'Brien. Also, because the hybridoma of Claim 63 has not been identified

by an ATCC No. as discussed supra, any hybridoma producing an antibody against a modified hepsin molecule is encompassed by the claim scope, and therefore anticipated by O'Brien.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 48-56, 58-61, 63-65 and 67-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mu et al. (US20030049645; published March 13, 2003; filed February 12, 2002; hereinafter referred to as "Mu") in view of Hellstrom et al. (USPN 5980896; published November 9, 1999; filed June 14, 1993; hereinafter referred to as "Hellstrom").

The interpretation of Claims 48-56, 58-61, 63-65 and 67-69 is discussed supra. Claim 59 is further drawn to doxorubicin, daunorubicin, taxol, ethidium bromide,

mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, dihydroxy anthracin dione, actinomycin D, abrin, and glucocorticoids. Claim 67 is further drawn to carriers of the pharmaceutical composition comprising: phosphate buffered saline solution, milk, clay, stearic acid or salts thereof, calcium stearate, and gums.

The interpretation of Mu is discussed supra. Mu does not disclose the following cytotoxic agents being conjugated to the antibody: doxorubicin, daunorubicin, taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, dihydroxy anthracin dione, actinomycin D, abrin, and glucocorticoids; and Mu does not disclose the following carriers comprising the pharmaceutical composition: phosphate buffered saline solution, milk, clay, stearic acid or salts thereof, calcium stearate, gums. Hellstrom rectifies these deficiencies in its disclosure.

Hellstrom discloses antibody conjugates useful for therapeutic applications as the antibody component of antibody-drug or antibody-toxin conjugates (Abstract) where the drug or toxin includes ricin and PE-antibodies (Col. 8, line 14); taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, actinomycin D, doxorubicin, daunorubicin, dihydroxy anthracin dione, glucocorticoids (Col. 13, lines 39-47); and abrin (Col. 20, line 57). Helstrom discloses pharmaceutical compositions comprising carriers including: phosphate buffered saline solution, water, emulsions such as oil/water emulsion, various types of wetting agents, starch, milk, sugar, certain types of clay, gelatin, stearic acid or salts thereof, magnesium or calcium stearate, talc, vegetable fats or oils, gums, glycols (Col. 14, lines 45-51).

It would have been *prima facie* obvious to have produced the instantly claimed antibody and pharmaceutical compositions in view of Mu and Hellstrom.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced the instant claimed antibody and pharmaceutical compositions in view of Mu and Hellstrom because Mu teaches in general the use of hepsin modulators (i.e., antibodies against hepsin protein fragments) for various applications relating to hepsin protein expression and protease activity involved in tumorigenesis and cancer progression and the need to identify compounds useful in the diagnosis, prevention and therapy of tumors. Hellstrom discloses immunoconjugates (Col. 13, lines 1-9; i.e., antibody conjugates) comprising immunotoxins comprising cytotoxic agents (Col. 3, line 20-48; Col. 13, line 39-47) and pharmaceutical compositions (Col. 14, lines 35-51). Because the antibodies were readily available at the time of the invention as disclosed by Mu, and methods for modifying antibodies to formulate immunoconjugates were known in the art as taught by Mu and Hellstrom, and which immunoconjugates or pharmaceutical compositions could further enhance the effects as taught by Mu and Hellstrom, one skilled in the art would have been motivated to have combined the reference disclosures in having been reasonably assured of success in producing antibody immunoconjuagtes and pharmaceutical compositions as those instantly claimed. Thus the claims were prima facie obvious over Mu and Hellstrom.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER